

USAMMDA INFORMATION PAPER

PRODUCT: *CAMPYLOBACTER* VACCINE (NV/SW)

DESCRIPTION: The *Campylobacter* vaccine is an oral, monovalent, killed whole-cell *Campylobacter jejuni* (strain 81-176) vaccine, combined with a modified *E. coli* heat-labile toxin adjuvant, LT(R192G). The adjuvant is a recombinantly produced, genetically modified, less-toxic form of the *E. coli* heat-labile enterotoxin, that enhances the ability of the vaccine to elicit an immune response at the mucosal surfaces of the intestinal tract. The vaccine has been developed through a Cooperative Research and Development Agreement with Antex Biologics, Inc. *Campylobacter* bacteria are a major cause of diarrheal illness in both the developed and developing world. The annual number of cases worldwide is estimated at 400 million; in the U.S., some 2.5 million cases occur annually. This disease causes as much as 14 percent of diarrheal illness worldwide, and *Campylobacter* enteritis is considered the severest form of traveler's diarrhea. *Campylobacter* bacteria cause diarrhea, abdominal cramps and pain (may mimic appendicitis), fever, nausea and vomiting. The diarrhea can be bloody (dysentery). The illness typically lasts from 2 to 10 days. Prolonged illness may occur in adults and relapses can happen. A typhoid fever-like syndrome or reactive arthritis may occur, and rarely, convulsions, Guillain-Barré syndrome (GBS) or meningitis. *Campylobacter* is consistently the most common cause of diarrhea among U.S. Forces participating in Operations Balance Torch and Cobra Gold in Southeast Asia.

PROGRAM RELEVANCE to the ARMY: This product supports both the core mission of the Army and the Army Transformation. Of the Army's core competencies, this product supports: "Shape the Security Environment," "Forcible Entry Operations," "Sustained Land Dominance" and "Support Civil Authorities" by protecting U.S. Forces against diarrheal illness caused by *Campylobacter* bacteria. The *Campylobacter* vaccine will enhance the sustainability of U.S. Forces in regions of the world where *Campylobacter* disease is endemic. In addition, this product supports Future Operational Capability MD97-007 (Preventive Medicine).

ISSUES/ ACTIONS:

- Data from a recent Phase 1 study suggest that a new lot of the killed, whole-cell *Campylobacter* (CWC) vaccine administered without adjuvant in a short-course, four-dose vaccine regimen may be as immunogenic and less reactogenic as the vaccine administered with adjuvant. However, vaccine-specific immune measures, fecal IgA and in vitro interferon-gamma, associated with protection in a volunteer experimental infection study trended toward higher levels of response in adjuvanted CWC vaccine recipients.
- Resource constraints as well as provision of proof of concept favor a Phase 2b inpatient challenge study over a Phase 2 field study. However, the use of live *Campylobacter* challenge strains may prove ethically unacceptable given concerns regarding risk of GBS with new data on in vivo/in vitro *C. jejuni* strain 81-176 lipooligosaccharide (LOS) phase variation. An alternative *C. jejuni* challenge strain that lacks ganglioside mimicry, such as an HS3 serotype is under evaluation in order to maintain a viable volunteer experimental infection model as a pivotal element of the *Campylobacter* vaccine clinical development program. Plan and conduct a Phase 2 dose-ranging study with an alternative *C. jejuni* strain for use in a CWC vaccine challenge study in FY04.
- The efficacy of a short-course, four-dose vaccine regimen has not been established. In addition, the requirement for the adjuvant must be evaluated. Plan and conduct a Phase 2 challenge study in US volunteers in FY05 applying the revised *C. jejuni* experimental infection model for proof of principle.
- The final vaccine formulation has not been determined. Devise and evaluate suitable alternatives to the current formulation (Antex Biologics, Inc., a subsidiary of Biopart Corporation) prior to Phase 3 efficacy studies.

BPL #: 196**DA PROJECT/TASK:** Infectious Diseases

PE/PROJ 643807.849ND

MAMP RANK: 5/36**ARMY ORD:** *Campylobacter* Vaccine; 23 Mar 95**SCHEDULE:**

MS I 4QFY94

MS II 3QFY97

MS FRP 1QFY06

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